

Application No. 10/814,025
Second Preliminary Amendment of June 3, 2004

Remarks

Claims 48-72 are active in this application. Claims 1-47 have been canceled. Claims 48-72 have been added. Applicant reserves the right to reintroduce the canceled claims in this or another application.

As set forth in the background of the invention, it has been found that naturally-occurring human placental glucocerebrosidase is not always delivered effectively to the phagocytic cells where it is active. The embodiments of the invention claimed herein address this problem and improve delivery to the phagocytic cells by providing glucocerebrosidase having a higher number exposed mannose residues than human placental glucocerebrosidase. Because phagocytes have mannose receptors that recognize glycoproteins with exposed mannose, glucocerebrosidase having a high number of exposed mannose residues has improved targeting to the phagocytic cells.

Accordingly, new claims 48-72 are directed to glucocerebrosidase having a higher number of exposed mannose residues than naturally occurring glucocerebrosidase purified from human placenta, methods for its production and methods for its use. Specifically, the new claims are directed to a method for producing glucocerebrosidase suitable for the treatment of Gaucher's disease in a human patient by treating a culture of mammalian cells capable of expressing glucocerebrosidase with an inhibitor of carbohydrate processing. The inhibitor acts to inhibit specific steps in the conversion of Glc₃Man₉GlcNac₂ to smaller species thus providing for a greater number of exposed mannose residues than human placental glucocerebrosidase. The applicants also present claims to a pharmaceutical composition comprising glucocerebrosidase with a higher number of exposed mannose residues and a method of treating a patient having Gaucher's disease with the glucocerebrosidase having a higher number of exposed mannose residues.

The newly added claims are fully supported by the specification as filed. For example, the specification at page 28, lines 4-11 specifically discloses treating cells capable of expressing glucocerebrosidase with "inhibitors of carbohydrate processing such as deoxy-mannojirimycin, swaisonine, castanospermine, deoxy-nojirimycin, N-methyl-deoxy-nojirimycin or their equivalent inhibitors. These inhibitors act to inhibit

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specific steps in the conversion of Glc₃Man₉GlcNac₂ smaller species shown in the figure, thus, providing a greater number of exposed mannose residues." Pharmaceutical compositions comprising such glucocerebrosidase molecules and methods of using such compositions to treat human patients with Gaucher's disease are clearly contemplated. No new matter has been introduced by this amendment. Accordingly, Applicants respectfully request that this amendment be entered.

If the Examiner believes that a telephone conference would expedite prosecution of this application, please telephone the undersigned.

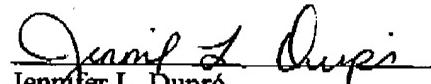
AUTHORIZATION FOR PAYMENT OF FEES

| Description | # Filed | # Allowed | # Extra | Rate | Fee |
|--------------------|---------|-----------|---------|-----------|----------------|
| Total Claims: | 25 | 20 | 5 | x \$18.00 | \$90.00 |
| Indep. Claims: | 3 | 3 | 0 | X \$84.00 | \$0.00 |
| TOTAL FEES: | | | | | \$90.00 |

If there are any charges, or any credits, please apply them to Deposit Account No. 07-1074.

Respectfully submitted,

Date: June 3, 2004


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